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| APPLICATION NO.                                | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/679,191                                     | 10/03/2003  | Randall T. Moon      | UWOTL121818         | 1034             |
| 26389  | 7590        | 05/11/2007           |                     |                  |
| CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC |             |                      | EXAMINER            |                  |
| 1420 FIFTH AVENUE                              |             |                      | SULLIVAN, DANIEL M  |                  |
| SUITE 2800                                     |             |                      |                     |                  |
| SEATTLE, WA 98101-2347                         |             |                      | ART UNIT            | PAPER NUMBER     |
|  |             |                      | 1636                |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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|------------------------------|---------------------------------------|------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/679,191  | <b>Applicant(s)</b><br>MOON ET AL. |  |
|                              | <b>Examiner</b><br>Daniel M. Sullivan | <b>Art Unit</b><br>1636            |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2007 and 08 March 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 9-33 is/are pending in the application.
- 4a) Of the above claim(s) 15-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-14 and 30-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

This Office Action is a reply to the Papers filed 11 January 2007 and 8 March 2007 in response to the Non-Final Office Action mailed 11 October 2006. Claims 15-29 were withdrawn from consideration and claims 9-14 and 30-33 were considered in the 11 October Office Action. Claims 9, 11, 13, 14, 30, 31, 32 and 33 were amended in the 8 March Paper. Claims 9-33 are pending and claims 9-14 and 30-33 are under consideration.

#### *Response to Amendment and Arguments*

##### Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-14 and 31-33 **stand rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons set forth in the 11 October Office Action at pages 4-7.

In response to the *prima facie* rejection of record, Applicant contends that claims 9 and 11 were amended to narrow their scope such that the second DNA segment encompasses nucleotide changes primarily in the promoter/enhancer region upstream from a functional reporter gene.

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This argument has been fully considered but is not deemed persuasive. The claims still allow for substantial variation within the promoter sequence while requiring that the modified nucleic acid maintain reporter function. As stated in the 11 October Office Action, the single species disclosed in the application is not representative of the broad genus claimed because it does not convey the necessary common attributes or features of any nucleic acid having the recited function and with regard to the “relevant identifying characteristics” of the claimed invention, the specification provides no disclosure of the structural features that define the function of a reporter of  $\beta$ -catenin and Lef dependent transcription. As stated in MPEP 2163(I)(A), a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes. Thus, applications that seek to claim biological molecules having a defined function and broadly divergent structure must disclose a correlation between that function and a corresponding structure. No such correlation is disclosed in the instant case and, therefore, the application also fails to provide the relevant identifying characteristics of the claimed invention.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention because it does not provide adequate written description for the broad class of any nucleic acid having 80% identity with any molecule comprising the sequence recited in the claim and the “same reporter function” of any DNA molecule comprising the recited sequence. Therefore, the claims are properly rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand properly rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description.

Claims 9-14 and 31-33 **stand rejected** under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell and transgenic zebrafish comprising a DNA molecule comprising nucleotides 3005-4336 of SEQ ID NO: 1 contiguous to nucleotides 1-243 of SEQ ID NO: 1, wherein the nucleic acid functions as a reporter of  $\beta$ -catenin and Lef dependent transcription, does not reasonably provide enablement for the broad scope of what is presently claimed. (See *supra*.) The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons set forth in the 11 October Office Action at pages 7-10.

In response to the *prima facie* rejection of record, Applicant contends that claims 9 and 11 were amended to narrow their scope such that the second DNA segment encompasses nucleotide changes primarily in the promoter/enhancer region upstream from a functional reporter gene.

This argument has been fully considered but is not deemed persuasive. As discussed above, the claims still allow for substantial variation within the promoter sequence while requiring that the modified nucleic acid maintain reporter function. Although the relative level of skill in the art is high, making the claimed invention would require undue experimentation. The claims are directed to a genus of cells and zebrafish comprising nucleic acids having broadly

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recited structural limitations. However, neither the relevant art nor the instant disclosure identifies the structural elements required to provide the function contemplated in the specification. Thus, the skilled artisan would not be able to distinguish the operative embodiments of the claimed invention from those that are inoperative without having to resort to empirical experimentation. Although the presence of inoperative embodiments within the scope of the claim does not necessarily render a claim non-enabled (see *Atlas Powder Co. v. E.I. du Pont de Nemours & Co* (224 USPQ 409, 414). *Atlas* also provides, “[o]f course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid” (page 414). In the instant case, the structural limitations recited in the claims encompass many thousands of possible combinations, and many, if not most of these combinations would be inoperative. As identifying the operative embodiments within the scope of the claims would require a large amount of empirical experimentation, the amount of experimentation required to make the full scope of the claimed invention would clearly be undue.

Applicant’s arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand properly rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Rejection of claims 9-14 and 31-33 under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth in the 11 October Office Action at page 11 is **withdrawn** in view of the claim amendments.

Claim Rejections - 35 USC § 102

Rejection of claims 9-11, 30 and 31 under 35 U.S.C. 102(a) as being clearly anticipated by Dorsky et al. (2002) *Dev. Biol.* 241:229-237 is **withdrawn** in view of the Declaration under 37-CFR 1.132 filed with the 11 January Paper.

Claim Rejections - 35 USC § 103

Rejection of claims 11-14 under 35 U.S.C. 103(a) as being unpatentable over Dorsky et al. (*supra*) in view of Talbot et al. (2000) *Genes Dev.* 14:755-762 is **withdrawn** in view of the Declaration under 37 CFR 1.132 filed with the 11 January Paper.

Rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Korinek et al. (1997) *Science* 275:1784-1787 in view of Li et al. (2000) US Patent No. 6,130,313 is **withdrawn**.

The claim was rejected under 35 U.S.C. §103(a) because although Korinek et al. taught a nucleic acid comprising the promoter sequence the promoter/enhancer region of the reporter vector pTOPFLASH (i.e., the segment 3005-3484 of the instant SEQ ID NO: 1), Korinek et al. failed to teach fusion of the promoter/enhancer to a nucleic acid encoding a destabilized GFP reporter gene (d2GFP). However, as amended, the host cell of claim 9 now encompasses a cell

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comprising any DNA segment which is at least 80% identical to the segment across nucleotides 3005-3484 of SEQ ID NO: 1, which encompasses any nucleic acid comprising the promoter/enhancer region of pTOPFLASH and having the same reporter and mRNA terminator function as a DNA segment consisting of 3005-4336 of SEQ ID NO: 1 contiguous to 1-243 of SEQ ID NO: 1. Thus, according to the limitations of the second DNA molecule, the claims now read on any cell comprising the TOPFLASH vector and are therefore anticipated by the teachings of Korinek et al. Accordingly, the rejection under 35 U.S.C. §103(a) is withdrawn in favor of the rejection under 35 U.S.C. §102(b) set forth herein below.

***New Grounds Necessitated by Amendment***

**Claim Rejections - 35 USC § 112, first paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-14 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The MPEP states, “[i]f new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. §112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).” (MPEP § 2163.06). The MPEP further states,



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“[w]henever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in the application” (*Id.*, § 2163.02). The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

In the instant case, the claims have been amended such that they are directed to a host cell transformed with a reported nucleic acid comprising a DNA segment which is at least 80% identical to a first DNA segment across a specifically defined region of SEQ ID NO: 1 from nucleotide 3005-3484, wherein the segment has the same reporter and mRNA terminator function as a segment consisting of nucleotides 3005-4336 of SEQ ID NO: 1 contiguous to nucleotides 1-243 of SEQ ID NO: 1.

The application as filed does not contemplate a genus of nucleic acid molecules defined as 80% identical to 3005-3484 of SEQ ID NO: 1 and having the same reporter and mRNA terminator function as a nucleic acid consisting of nucleotides 3005-4336 of SEQ ID NO: 1 contiguous to nucleotides 1-243 of SEQ ID NO: 1. Instead, the application (e.g., originally filed claim 1) describes a DNA molecule having at least 80% identity and the same reporter function as a DNA molecule comprising nucleotides 3005-4336 of SEQ ID NO: 1 contiguous to

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nucleotides 1-243 of SEQ ID NO: 1. As the structural limitation 80% identical to 3005-3484 of SEQ ID NO: 1 defines a genus that is substantially different from the genus defined as 80% identical to nucleotides 3005-4436 contiguous with 1-233 of SEQ ID NO: 1, the scope of the genus now claimed is substantially different from the genus disclosed in the previous Application. Furthermore, the application as filed does not teach a nucleic acid molecule limited to having the same mRNA terminator function as a DNA segment consisting of nucleotides 3005-4436 contiguous with 1-233 of SEQ ID NO: 1. Therefore, the limitation is clearly not supported by the original disclosure.

Thus, the amended claims are now directed to subject matter that is neither explicitly nor implicitly disclosed in the originally filed application. Therefore, the claims contain impermissible new matter.

#### Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Korinek et al. (1997) *Science* 275:1784-1787 (of record) as evidenced by the pcDNA1/Neo Vector, Datasheet [online], Invitrogen Life Technol, [retrieved on 7 May 2007]. Retrieved from the Internet: URL: [www.invitrogen.com/content/sfs/vectors/pcdna1neo.pdf](http://www.invitrogen.com/content/sfs/vectors/pcdna1neo.pdf).

As described above, as amended, the host cell of claim 9 now encompasses a cell comprising any DNA segment which is at least 80% identical to the segment across nucleotides 3005-3484 of SEQ ID NO: 1 (i.e., the promoter/enhancer region of pTOPFLASH). Thus, according to the limitations of the second DNA molecule, the claims now read on any cell comprising the TOPFLASH vector and a reporter gene and are therefore anticipated by the teachings of Korinek et al. who teaches the construction of the pTOPFLASH vector comprising the promoter/enhancer region fused to a luciferase reporter gene. (See especially p. 1786, ll. 2-10.) Korinek et al. further teaches the use of the pTOPFLASH vector in cellular assays for  $\beta$ -catenin and TCF activity. (See especially Fig. 3 and the caption thereto.) Thus, the DNA segment of Korinek et al. has the same reporter activity as the first DNA segment (i.e., it can be used as a reporter of  $\beta$ -catenin and TCF activity). With regard to the limitation that the DNA segment have the same mRNA terminator function, Korinek teaches that the TOPFLASH vector was constructed from the vector pcDNA (see especially footnote 14), which the Invitrogen Life Technologies product description evidences contains an SV40 polyadenylation signal mRNA terminator sequence (labeled SV40 intron/pA on the plasmid map).

Therefore, the host cell of Korinek et al. comprises all of the elements of the host cell of the instant claim.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel M Sullivan, Ph.D.  
Primary Examiner  
Art Unit 1636

